IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF NORTH CAROLINA
Durham Division

VICTOR VOE, *et al.*, *Plaintiffs*, v. THOMAS MANSFIELD, *et al.*, *Defendants*, and PHILIP E. BERGER, *et al.*, *Intervenor-Defendants*.	Civil No. 1:23-CV-864-LCB-LPA

EXPERT REBUTTAL DECLARATION OF DAN H. KARASIC, M.D.

I, Dan H. Karasic, M.D., hereby declare and state as follows:

1. I am over 18 years of age, of sound mind, and in all respects competent to testify.

2. I have been retained by counsel for Plaintiffs as an expert in connection with the above-captioned litigation.

3. I have actual knowledge of the matters stated herein. If called to testify in this matter, I would testify truthfully and based on my expert opinion.

4. I incorporate as part of this rebuttal declaration my opinions and qualifications as set forth in my initial expert declaration in this matter, which is dated October 6, 2023 and was filed on October 11, 2023.

5. I submit this rebuttal declaration to respond to the expert declaration of Dr. James Cantor, including attachments,[1] as well as statements made in the Intervenor-Defendants' Response in Opposition to Plaintiffs' Motion for Preliminary Injunction (the "Response").

6. In this rebuttal, I respond to some of the central points made in Dr. Cantor's declaration and the Response. I do not address each and every assertion made in those documents that I believe are baseless, misleading, or mischaracterizations of the evidence, as there are many. Instead, my aim is to provide an explanation of the erroneous premises upon which their conclusions are based.

7. In preparing this rebuttal declaration, I relied on my training and years of research and clinical experience, as set out in my curriculum vitae attached to my initial expert declaration, and on the materials listed therein; the materials referenced in my initial declaration and listed in the bibliography attached thereto; and on the materials referenced herein and the supplemental bibliography attached as **Exhibit C**. I reserve the

[1] Dr. Cantor is well known for his work with paraphilias, and in particular with pedophiles, but not for his work with transgender people. Paraphilias are persistent and recurrent sexual interests, urges, fantasies, or behaviors of marked intensity involving objects, activities, or even situations that are atypical in nature. Being transgender is not a paraphilic disorder.

right to revise and supplement the opinions expressed in this report or the bases for them if any new information becomes available in the future, including as a result of new scientific research or publications or in response to statements and issues that may arise in my area of expertise.

REBUTTAL OPINIONS

A. GENDER DYSPHORIA IS A MEDICAL CONDITION

8. Gender Dysphoria is a serious medical condition that warrants medical treatment when appropriate. It is characterized by the distress resulting from the misalignment between a person's gender identity, which has biological bases, and their body (i.e., physical characteristics). Gender dysphoria is listed as a mental disorder in the Diagnostic and Statistical Manual of Mental Disorders, the DSM-5-TR, because the diagnosis focuses on the significant distress resulting between the incongruence between one's gender identity and body, Gender Incongruence is listed outside of the mental disorders section in the International Classification of Diseases, ICD-11, in recognition of its status as a medical condition that may require treatment with medication and surgery. Dr. Cantor's assertion that "Gender dysphoria is nowhere defined as a medical … diagnosis" (Cantor ¶ 109) is thus inaccurate.

9. In my over thirty years of clinical experience working with thousands of adolescents and young adults with gender dysphoria, psychotherapy has been a central part of treating minors with gender dysphoria, as it is with many conditions; and diagnosing and treating gender dysphoria involves careful assessment, differential

diagnosis and management of comorbid conditions. Though psychotherapy can be a critical part of managing a patient's well-being, psychotherapy is not sufficient for those needing medical intervention to treat the patient's dysphoria which stems from the incongruence between a patient's physiological sex-based characteristic and gender identity.

B. Gender dysphoria is not subjective diagnosis.

10. Dr. Cantor seems to imply that medical treatment should not be provided to transgender adolescents because, according to him, "Gender identity refers to subjective feelings that cannot be defined, measured, or verified by science." (Cantor ¶ 108). This is incorrect. A patient may self-report their gender identity, but Gender Dysphoria is a well-recognized medical diagnosis made by a clinician. Indeed, clinical interviews with patients are typically used to diagnose other DSM and non-DSM diagnoses and determine treatment. This widely used assessment tool is not unique to gender dysphoria.

11. As a psychologist, Dr. Cantor must know that most DSM-5 psychiatric diagnoses are made via an evaluation which may include, among other things, the psychiatric interview of the patient, a review of records, and an interview with parents in the case of a minor patient. The diagnosis of Gender Dysphoria under the DSM-5 is made the same way as other DSM diagnoses, through an evaluation in which the health professional determines if DSM-5 diagnostic criteria are met. Mental health professionals are well-trained to conduct such interviews. The validity and reliability of DSM-5 diagnoses were assessed and determined in the process of creating the DSM-5. Clinicians

do not simply defer to the reported experiences of the patient, but instead rely on the application of professional experience and expertise to assess whether the patient meets the relevant diagnostic criteria. Similarly, the ICD-11 diagnosis of Gender Incongruence is made by an evaluation which includes an interview of the patient. The World Health Organization conducted field studies internationally on the reliability and validity of the Gender Incongruence diagnosis of ICD-11. (de Vries, et al 2021).

C. Dr. Cantor offers no alternative effective treatment for adolescents with gender dysphoria.

12. Dr. Cantor disapproves of existing protocols for treating gender dysphoria in adolescents, but he offers no alternative treatments for this condition, let alone ones supported by the evidentiary standards he holds the existing protocols to.

13. Psychotherapy generally is certainly appropriate and is an aspect of care for children and adolescents with gender dysphoria. But those types of interventions do not resolve the dysphoria when medical interventions are indicated and are not alternatives to medical interventions for adolescents who need them. My initial declaration discusses the harms that can result from the denial of medically indicated gender-affirming medical care.

14. Dr. Cantor discusses the "Dutch Protocol" as if it were an alternative treatment approach to the existing treatment paradigms outlined in the WPATH SOC 7, WPATH SOC 8, and the Endocrine Society Guideline. (*See* Cantor ¶¶ 239-47). The Dutch team defines "the Dutch Protocol [as] consisting of a gonadotropin-releasing hormone agonist (GnRHa) to halt puberty and subsequent gender-affirming hormones

(GAHs) … implemented to treat adolescents with gender dysphoria." (van der Loos, 2023). The Dutch team states that for "prepubertal children [the team] adopted a "watchful waiting" approach. This approach meant that the child returned to the gender identity clinic only when puberty had begun. The child was not seen in the meanwhile because medical intervention is not provided to prepubertal children at our clinic." While there are studies finding that many prepubertal children diagnosed with Gender Identity Disorder (a precursor diagnosis to Gender Dysphoria in Children) identified with their sex assigned at birth at a later follow up, gender dysphoria that continues into adolescence is very unlikely to desist. (DeVries, et al., 2011, Wiepjies, et al. 2018, Brik, et al., 2020). Hence, the Dutch researchers who coined the term "watchful waiting" for prepubertal children also did the seminal research on medical interventions for those patients whose gender dysphoria persists until adolescence. (de Vries, 2011; Steensma, 2011; de Vries, 2014).

15. There is likewise no basis for suggesting that providing gender-affirming care will cause youth with gender dysphoria who would otherwise desist to, instead, persist. This claim erroneously relies on the assertion that social transition in prepubertal children can cause their gender dysphoria to persist into adolescence. First, the fact that there is a correlation between social transition prior to puberty and persistence does not establish that social transition causes persistence of gender dysphoria. The intensity of gender dysphoria prior to puberty predicted persistence, and children with more intense dysphoria were more likely to socially transition. (Steensma, 2013). Rae, et al. (2019)

found that "stronger cross-sex identification and preferences expressed by gender-nonconforming children at initial testing predicted whether they later socially transitioned." Regardless of what conclusions can be drawn from these desistance studies about the impact of gender affirmation on the persistence rates in prepubertal children, this research does not apply to adolescents with gender dysphoria, for whom desistance is rare, and the treatments banned by HB 808 are not indicated until adolescence.

16. The suggestion that adolescents can just wait until they are 18 years old to get care ignores the harm of not providing the care. Allowing endogenous puberty to advance is not a neutral decision. For many adolescents, the development of secondary sex characteristics that do not match their gender identity can have a severe negative impact on their mental health and can exacerbate lifelong dysphoria because some of those characteristics are impossible to change later through surgeries. In addition, youth may suffer needlessly from untreated gender dysphoria while waiting to turn 18.

D. Dr. Cantor's critique regarding systematic reviews.

17. Dr. Cantor refers to purported systematic reviews of the literature examining gender-affirming care for minors to argue that there is not sufficient evidence supporting the provision of this care.

18. But, with the exception of the Swedish review, which was commissioned by a government agency and later published (Ludvigsson, et al., 2023), the reviews upon which Dr. Cantor relies are reports authored or commissioned by government committees that have not been published in any medical or scientific journals and have not been

subjected to the peer-review process. Moreover, some of these reports do not include the most recent research demonstrating the efficacy of the banned treatments and others do not address all the relevant literature.

19. Further, it is important to put GRADE scores of systematic reviews in context. Only a small percentage of systematic reviews of medical interventions have a high GRADE score; for a majority of systematic reviews of medical interventions, GRADE scores are low or very low. (Fleming et al., 2016, Howick, et al., 2020). For complex interventions, for which gender affirming care certainly qualifies, no high GRADE scores were found for systematic reviews of any complex intervention. (Movsisyan, et al., 2016).

20. If only medical interventions with high GRADE scores were permitted by law, most medical interventions and all complex interventions would be banned. In a study of systematic reviews of interventions in anesthesiology, critical care medicine, and emergency medicine, only 10% had high GRADE scores, but banning the practice of anesthesiology, critical care medicine, and emergency medicine has not been contemplated (Conway, et al, 2017). Chong, et al., 2023 found that only 36% of national guidelines for care were based on strong or moderate GRADE scores. Recommendations are based on a comparison with alternatives; there is no evidence base to support conversion therapy or other psychotherapeutic interventions as an alternative for those who need gender-affirming medical treatment.

21. Many treatments for other conditions are widely accepted and in use without having been studied through randomized, controlled clinical trials. And many drugs for cancer and hematologic disorders have been FDA approved without a randomized controlled trial (Hatswell, et al., 2016). Other drugs have been FDA approved with randomized controlled trials for one indication but are commonly used for another condition or in a different population than the one for which it was approved (Wittich, et. al., 2012).

22. Dr. Cantor relies heavily on a so-called "systematic review of systematic reviews" authored by Romina Brignardello-Petersen and Wojtek Wiercioch. This "review" was commissioned by Florida Agency for Health Care Administration in support of its since invalidated rule prohibiting Medicaid coverage for medical treatment of gender dysphoria.[2]

23. Brignardello-Petersen and Wiercioch performed a manual search of websites that includes only one non-governmental organization site: the Society for Evidence-Based Gender Medicine (SEGM). The fact that SEGM was chosen instead of much larger and more established organizations representing the mainstream of care, e.g., the American Psychological Association, the American Medical Association, or the

[2] Dr. Brignardello-Petersen is a dentist who is an assistant professor in the Department of Health Research Methods, Evidence, and Impact at McMaster University in Canada. Dr. Wiercioch is a post-doctoral research fellow in the same department as Dr. Brignardello-Petersen. Both authors report no academic interests in the care of people with gender dysphoria.

American Psychiatric Association, raises a concern for bias, as SEGM is a small group founded recently specifically in opposition to gender-affirming care. Of note, Brignardello-Petersen disclosed at the 2023 SEGM conference that SEGM is funding her systematic reviews.

24. Even then the review by Brignardello-Petersen and Wiercioch still found that that "Low certainty evidence suggests that after treatment with puberty blockers, people with gender dysphoria experience a slight increase in gender dysphoria, and *an improvement in depression, and anxiety*." Similarly, it found that "Low certainty evidence suggests that after treatment with cross-sex hormones, people with gender dysphoria experience *an improvement in gender dysphoria, depression, anxiety, and suicidality*."

E. Dr. Cantor's critiques of specific studies are baseless.

25. Dr. Cantor cites a Finnish study as evidence for his conclusion that adolescents should not be prescribed gender-affirming hormones because they are supposedly not effective in the treatment of gender dysphoria. (Kaltiala, et al, 2020). However, in that study, the need for treatment for depression dropped from 54% of the youth to 15%; the need for treatment for anxiety dropped from 48% of the youth to 15%; and the need for treatment for suicidality/self-harm dropped from 35% to 4%. All of these were statistically highly significant changes.

26. Dr. Cantor states that the study by Kuper, et al. 2020 did not show benefit from treatment. This statement is misleading at best. The article concludes, "Youth

reported large improvements in body dissatisfaction (P < .001), small to moderate improvements in self-report of depressive symptoms (P < .001), and small improvements in total anxiety symptoms (P < .01)." (Kuper, et al., 2020). Dr. Cantor further states that the study by Achille et al. does not show that those studied benefitted from endocrine treatment. Again, Dr. Cantor's characterization of this study's conclusion is misleading. The results of the paper actually show that, "Mean depression scores and suicidal ideation decreased over time while mean quality of life scores improved over time. When controlling for psychiatric medications and engagement in counseling, regression analysis suggested improvement with endocrine intervention. This reached significance in male-to-female participants." (Achille, et al., 2020).

F. Dr. Cantor's claim that there is an international consensus against the provision of gender-affirming medical is not accurate.

27. Dr. Cantor claims that prohibiting gender-affirming medical treatment for transgender adolescents with gender dysphoria is consistent with a so-called international consensus. This is completely false. None of the countries to which Dr. Cantor refers has banned gender-affirming medical care for adolescents with gender dysphoria as North Carolina's ban does. To the contrary, all agree that medical treatment, including puberty blockers and hormone therapy, are appropriate in some circumstances.

28. Dr. Cantor refers to an interim report on care of transgender youth in the United Kingdom's National Health System which is compiled by Dr. Hilary Cass. The interim report states that the final report will synthesize published evidence with expert opinion and stakeholder input. Notably, the interim report recommends increasing the

number of health providers, shortening wait times, and increasing the number of centers across the country providing care to transgender youth.

29. Swedish, Norwegian, and Finnish national health authorities, which Dr. Cantor also references, have recommended more research but have not banned care for transgender youth. In Sweden, one of the six gender centers caring for transgender adolescents stopped taking new patients in 2021 until new national guidelines were released in 2022, but continued to provide care to those already in treatment, and new patients were accepted at other gender centers. After the national guidelines were released, care to new patients resumed at that gender center, and continued to be provided at the other gender centers. In these countries, gender-affirming care for adults and for youth who qualify is fully paid for by the national health system of each country. Cantor states that Finland halted surgery for trans youth in 2020, but surgery was already restricted there to those 18 and over, while puberty blockers and hormones remain available when clinicians deem them necessary.

30. The provision of care for transgender youth has not been limited in France.

31. Gender-affirming care continues to be provided by teams of gender affirming care providers across Europe, as demonstrated by the sessions at the 2023 European Professional Association for Transgender Health conference. Thomas Steensma of the Dutch research team has explicitly rejected the concepts of Rapid Onset Gender Dysphoria and social contagion that have been used by opponents of gender affirming care for minors (Broderick, 2023). Dr. Cantor does not provide care for gender

dysphoric youth in his home country of Canada, but such care is widely available and not restricted in Canada. Gender-affirming care for youth remains available in other parts of the world, including Australia, New Zealand, South Africa, Uruguay, Argentina, Brazil, Chile, and Israel. The outliers that ban gender-affirming medical care for minors are some American states, as well as Russia.

32. There remains strong international support for the continued provision of gender-affirming medical and surgical care. Experts from around the world have collaborated on the new WPATH Standards of Care Version 8. I was chapter lead of the Mental Health chapter of this version, and the authors of that chapter include psychiatrists who are leaders of transgender health programs in Belgium, Sweden, and Turkey. There is broad agreement in philosophy of care, including support for gender-affirming care and opposition to conversion therapy.

G. Dr. Cantor draws inappropriate conclusions from the numbers and sex ratios of gender clinic referrals.

33. Dr. Cantor devotes many pages to the increase in the numbers of referrals to gender clinics, and changes in sex ratios of patients, to the extent that he considers it a distinct phenomenon called "adolescent-onset gender dysphoria." (*See*, *e.g.*, Cantor ¶¶ 17, 25, 33, 136-38). As an initial matter, in his caricature of doctors pushing medical transition (or what he calls "affirmation-on-demand," *see* Cantor ¶ 256), Dr. Cantor seems to imply the field is ignoring and avoiding exploration of these developments. That is not the case. Indeed, the chapter on adolescents in WPATH SOC 8 specifically discusses the

increase in referrals to gender clinics and the sex ratios of these young patients. (*See* WPATH SOC 8 at Chapter 6).

34. In support for his proposition that "adolescent-onset gender dysphoria" is a distinct phenomenon, Dr. Cantor relies and cites to cites a survey by Lisa Littman of participants on discussion websites for parents who opposed their children's gender transition and derived a theory that adolescents develop gender dysphoria via social contagion. This survey has been denounced by the World Professional Association for Transgender Health. The survey was of parents' perception after learning of their children's transgender identity, rather than of the children themselves, and conflicts with the experience of those who work with the children themselves. No conclusions can be drawn from the Littman survey other than the fact that some anonymous people recruited from internet sites who opposed transition care for youth speculate that transgender identity is due to social contagion. No study to date has demonstrated that the determinant of gender identity is psychosocial.

35. Dr. Cantor seems to attribute increases in youth experiencing gender dysphoria to "the introduction of social media." (Cantor ¶ 258). But the rise in numbers of referrals is hardly surprising given the greater awareness on the part of youth and their parents of what gender dysphoria is and that care is available, as well as the significant increase in the number of clinics available to provide care. In addition, the stigma associated with being transgender, while still significant, has lessened in recent years. Coming out to parents and seeking care are options that did not exist for many youth until

recently, so an increase in numbers of referrals to gender clinics is not surprising. While there is a documented increase in clinic referrals, Dr. Cantor exaggerates the increase by making inappropriate comparisons.

36. Until the past decade, little data on the number of people identifying as transgender was available. From 2007 to 2009, a question asking whether the respondent identified as transgender was added to a large population-based health survey conducted in Massachusetts, and 0.5% of study participants identified as transgender. (Conron, et al., 2012). Since then, this question was added to large health surveys in other states, and analyses of surveys done in 2014 found that, nationally, 0.5-0.6% of adults identified as transgender, and 0.7% of youth ages 13 to 17 identified as transgender. (Crissman, et al., 2017; Flores, et al., 2016; Herman, et al., 2017).

37. While increases in numbers and changes in sex ratios of patients referred to some gender clinics have been reported, since the number of patients referred to gender clinics reflect only a small fraction of the people identifying as transgender, these changes may reflect changes in referral patterns to clinics rather than changes in the number of people identifying as transgender.

38. Sex ratios of patients vary from clinic to clinic and over time. When I was the psychiatrist for the Dimensions Clinic for transgender youth in San Francisco from 2003 to 2020, a consistent majority of my patients were assigned female at birth. Other clinics have had more assigned male at birth patients. The rise in numbers and percentage of patients assigned female at birth observed at some clinics in recent years is not

surprising given the historical development of the study of gender dysphoria in youth. The first large American study of gender non-conforming youth was the Feminine Boy Study at UCLA. There was significant societal discomfort with and rejection of boys who departed from sex stereotypes—the director of the study referred to them as "sissy boys" in the book resulting from the study—and these boys often experienced bullying from peers. In this context, boys who were perceived to be effeminate were the population brought in to psychiatrists by their parents and were the population that was initially studied by researchers. (Green, 1987). Parents were not as concerned about gender non-conforming girls as they were more socially accepted. There was also less awareness among the general public of the existence of transgender males and that transitioning was an option for individuals assigned female at birth who were experiencing gender dysphoria. The increase in awareness in recent decades made it possible for individuals who ultimately came to identify as transgender men to come out and seek care.

39. Ultimately, the diagnostic criteria for gender dysphoria are rigorous: if there were individuals claiming a transgender identity to fit into a peer group, they would not meet the criteria for a gender dysphoria diagnosis, let alone be deemed to need medical interventions.

H. Dr. Cantor's assessment of risks is based on baseless speculation.

40. Dr. Cantor speculates at length on the safety and efficacy of puberty blockers and hormones in gender dysphoric youth. The Endocrine Society and the Pediatric Endocrine Society have replied to efforts to limit care for youth by re-asserting

that these treatments are safe and effective, and that treating gender dysphoria in youth has substantial health benefits. (e.g., Endocrine Society, 2022).

41. Dr. Cantor makes misleading assertions about Kuper, et al, 2020's findings on gender-affirming care and suicidal ideation and attempts. Dr. Cantor says Kuper shows increased suicidal ideation and attempts after treatment than before—but the suicidality listed was for the 1-3 months before starting treatment compared to a much longer period 11-18 months after treatment, so of course more suicidality was recorded over a much longer period. The participants in Kuper showed benefit from treatment: a great improvement in body congruence.

42. Dr. Cantor states that Dhejne et al., supports increased suicidality in those who had gender affirming surgery—but this comparison is with the general population. There were 10 suicides in the national morbidity and mortality database involving trans people over a 30-year period, compared to 5 suicides in from the general population. The paper itself cautions against using this study as evidence of the effect of surgery on suicide. And Cecilia Dhejne has specifically called out misrepresentations of her study, stating: "The findings have been used to argue that gender-affirming treatment should be stopped since it could be dangerous (Levine, 2016) … Despite the paper clearly stating that the study was not designed to evaluate whether or not gender-affirming treatment is beneficial, it has been interpreted as such." (Dhejne, 2017).

43. Dr. Cantor states "No methodologically sound studies have provided meaningful evidence that medical transition reduces suicidality in minors." However,

Kaltiala, et al. (2020), which is cited several times in Cantor's declaration in support of his assertions, and therefore presumably considered by Cantor a methodologically sound study, found that dramatically fewer youth (35% vs 4%) needed treatment for suicidality after starting gender-affirming hormones.

I. Gender-affirming medical care has long term benefits.

44. I have treated people ranging from adolescents to elders. And many of my patients have remained with me for decades, e.g., where a patient is on medications that need to be monitored, and their medical transition was a positive health care decision not just in the short term but for the course of their lives.

45. Dr. Cantor's assertions regarding the incidence of regret and "detransition" are inconsistent with the data and my clinical experience. (*See* Cantor ¶¶ 125, 224). A study of all individuals receiving gender-affirming surgery in Sweden over 50 years (1960 to 2010) found a regret rate of 2.2.%, a percentage that only declined over the years. There were ten cases of regret from 1960 to 1980, and only five cases of regret total in the last 30 years that were reviewed, from 1981-2010. (Dhejne, et al., 2014). A meta-analysis of 27 studies which reported regret after gender-affirming surgery found that of 7928 people having gender-affirming surgery, the regret rate was 1%. (Bustos, et al., 2021).

46. In my experience, I have had some patients who halted their transition due to challenging personal circumstances—e.g., fear of losing family support— but they still had gender dysphoria. And some came back years later to resume their transition. I have also had patients discontinue medical treatment for other reasons, including being happy

with the existing changes and continuing to live and identify as transgender. But in 30 years, I have never seen a patient who had undergone hormone therapy and surgery and later came to identify with their sex assigned at birth and regret the treatment they had received.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Executed this 16th day of November 2023.

Dan H. Karasic, M.D.

Exhibit C

SUPPLEMENTAL BIBLIOGRAPHY

Achille, C., Taggart, T., Eaton, N. R., Osipoff, J., Tafuri, K., Lane, A., & Wilson, T. A. (2020). Longitudinal impact of gender-affirming endocrine intervention on the mental health and well-being of transgender youths: preliminary results. *International journal of pediatric endocrinology*, *2020*, 8.

American Psychiatric Association. (2022). Diagnostic and statistical manual of mental disorders (5th ed., text rev.). Arlington, VA: American Psychiatric Publishing.

Brik, T., Vrouenraets, L. J. J. J., de Vries, M. C., & Hannema, S. E. (2020). Trajectories of Adolescents Treated with Gonadotropin-Releasing Hormone Analogues for Gender Dysphoria. *Archives of sexual behavior*, *49*(7), 2611–2618.

Broderick, Timmy. "Evidence Undermines 'Rapid Onset Gender Dysphoria' Claims," Scientific American (Aug. 24, 2023), https://www.scientificamerican.com/article/evidence-undermines-rapid-onset-gender-dysphoria-claims/.

Bustos, V. P., Bustos, S. S., Mascaro, A., Del Corral, G., Forte, A. J., Ciudad, P., Kim, E. A., Langstein, H. N., & Manrique, O. J. (2021). Regret after Gender-affirmation Surgery: A Systematic Review and Meta-analysis of Prevalence. *Plastic and reconstructive surgery. Global open*, *9*(3), e3477.

Chong, M.C., Sharp, M.K., Smith, S.M. *et al.* (2023). Strong recommendations from low certainty evidence: a cross-sectional analysis of a suite of national guidelines. *BMC Med Res Methodol* 23, 68.

Coleman, E., Radix, A. E., Bouman, W. P., Brown, G. R., de Vries, A. L. C., Deutsch, M. B., Ettner, R., Fraser, L., Goodman, M., Green, J., Hancock, A. B., Johnson, T. W., Karasic, D. H., Knudson, G. A., Leibowitz, S. F., Meyer-Bahlburg, H. F. L., Monstrey, S. J., Motmans, J., Nahata, L., Nieder, T. O., … Arcelus, J. (2022). Standards of Care for the Health of Transgender and Gender Diverse People, Version 8. *International journal of transgender health*, *23*(Suppl 1), S1–S259.

Coleman, E., Bockting, W., Botzer, M., Cohen-Kettenis, P., DeCuypere, G., Feldman, J., ... & Zucker, K. (2012). Standards of care for the health of transsexual, transgender, and gender-nonconforming people, version 7. *International Journal of Transgenderism*, 13(4), 165-232.

Conron, K. J., Scott, G., Stowell, G. S., & Landers, S. J. (2012). Transgender health in Massachusetts: results from a household probability sample of adults. *American journal of public health*, *102*(1), 118–122.

Conway, A., Conway, Z., Soalheira, K., & Sutherland, J. (2017). High quality of evidence is uncommon in Cochrane systematic reviews in Anaesthesia, Critical Care and Emergency Medicine. *European journal of anaesthesiology*, *34*(12), 808–813.

Crissman, H. P., Berger, M. B., Graham, L. F., & Dalton, V. K. (2017). Transgender Demographics: A Household Probability Sample of US Adults, 2014. *American journal of public health*, *107*(2), 213–215.

de Vries, A. L. C., Beek, T. F., Dhondt, K., de Vet, H. C. W., Cohen-Kettenis, P. T., Steensma, T. D., & Kreukels, B. P. C. (2021). Reliability and Clinical Utility of Gender Identity-Related Diagnoses: Comparisons Between the ICD-11, ICD-10, DSM-IV, and DSM-5. *LGBT health*, *8*(2), 133–142.

de Vries, A. L. C., McGuire, J. K., Steensma, T. D., Wagenaar, E. C. F., Doreleijers, T. A. H., & Cohen-Kettenis, P. T. (2014). Young Adult Psychological Outcome After Puberty Suppression and Gender Reassignment. *Pediatrics*, *134*(4), 696-704.

de Vries, A. L., Steensma, T. D., Doreleijers, T. A., & Cohen-Kettenis, P. T. (2011). Puberty suppression in adolescents with gender identity disorder: a prospective follow-up study. *The journal of sexual medicine*, *8*(8), 2276–2283.

Dhejne, C. H. (2017). Science AMA Series: I'm Cecilia Dhejne a fellow of the European Committee of Sexual Medicine, from the Karolinska University Hospital in Sweden. I'm here to talk about transgender health, suicide rates, and my often misinterpreted study. Ask me anything! *Winnower* 10:e150124.46274.

Dhejne, C., Öberg, K., Arver, S., & Landén, M. (2014). An analysis of all applications for sex reassignment surgery in Sweden, 1960-2010: prevalence, incidence, and regrets. *Archives of sexual behavior*, *43*(8), 1535–1545.

Dhejne, C., Lichtenstein, P., Boman, M., Johansson, A. L., Långström, N., & Landén, M. (2011). Long-term follow-up of transsexual persons undergoing sex reassignment surgery: cohort study in Sweden. *PloS one*, *6*(2), e16885.

Endocrine Society. Press release: Endocrine Society alarmed at criminalization of transgender medicine (Feb. 23, 2022). Available from https://www.endocrine.org/news-and-advocacy/news-room/2022/endocrine-society-alarmed-at-criminalization-of-transgender-medicine.

Fleming, P. S., Koletsi, D., Ioannidis, J. P., & Pandis, N. (2016). High quality of the evidence for medical and other health-related interventions was uncommon in Cochrane systematic reviews. *Journal of clinical epidemiology*, *78*, 34–42.

Flores, A.R., Herman, J.L., Gates, G.J., & Brown, T.N.T. (2016). How Many Adults Identify as Transgender in the United States? Los Angeles, CA: The Williams Institute. Retrieved from https://escholarship.org/uc/item/2kg9x2rk.

Green, R. (1987). The "sissy boy syndrome" and the development of homosexuality. Yale University Press.

Hatswell, A. J., Baio, G., Berlin, J. A., Irs, A., & Freemantle, N. (2016). Regulatory approval of pharmaceuticals without a randomised controlled study: analysis of EMA and FDA approvals 1999-2014. *BMJ open*, *6*(6), e011666.

Hembree, W. C., Cohen-Kettenis, P. T., Gooren, L., Hannema, S. E., Meyer, W. J., Murad, M. H., Rosenthal, S. M., Safer, J. D., Tangpricha, V., & T'Sjoen, G. G. (2017). Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *The Journal of clinical endocrinology and metabolism*, *102*(11), 3869–3903.

Herman, J. (2013). Costs and Benefits of Providing Transition-related Health Care Coverage in Employee Health Benefits Plans: Findings from a Survey of Employers. UCLA: The Williams Institute. Retrieved from https://escholarship.org/uc/item/5z.

Howick, J., Koletsi, D., Pandis, N., Fleming, P. S., Loef, M., Walach, H., Schmidt, S., & Ioannidis, J. P. A. (2020). The quality of evidence for medical interventions does not improve or worsen: a metaepidemiological study of Cochrane reviews. *Journal of clinical epidemiology*, *126*, 154–159.

Kaltiala, R., Heino, E., Työläjärvi, M., & Suomalainen, L. (2020). Adolescent development and psychosocial functioning after starting cross-sex hormones for gender dysphoria. *Nordic journal of psychiatry*, *74*(3), 213–219.

Kuper, L. E., Stewart, S., Preston, S., Lau, M., & Lopez, X. (2020). Body Dissatisfaction and Mental Health Outcomes of Youth on Gender-Affirming Hormone Therapy. *Pediatrics*, *145*(4), e20193006.

Ludvigsson, J. F., Adolfsson, J., Höistad, M., Rydelius, P. A., Kriström, B., & Landén, M. (2023). A systematic review of hormone treatment for children with gender dysphoria and recommendations for research. *Acta paediatrica*, *112*(11), 2279–2292.

Movsisyan, A., Melendez-Torres, G. J., & Montgomery, P. (2016). Outcomes in systematic reviews of complex interventions never reached "high" GRADE ratings when compared with those of simple interventions. *Journal of clinical epidemiology*, *78*, 22–33.

Rae, J. R., Gülgöz, S., Durwood, L., DeMeules, M., Lowe, R., Lindquist, G., & Olson, K. R. (2019). Predicting Early-Childhood Gender Transitions. *Psychological science*, *30*(5), 669–681.

Steensma, T. D., McGuire, J. K., Kreukels, B. P., Beekman, A. J., & Cohen-Kettenis, P. T. (2013). Factors associated with desistence and persistence of childhood gender dysphoria: a quantitative follow-up study. *Journal of the American Academy of Child and Adolescent Psychiatry*, *52*(6), 582–590.

Steensma, T. D., Biemond, R., de Boer, F., & Cohen-Kettenis, P. T. (2011). Desisting and persisting gender dysphoria after childhood: a qualitative follow-up study. *Clinical child psychology and psychiatry*, *16*(4), 499–516.

van der Loos, M. A. T. C., Klink, D. T., Hannema, S. E., Bruinsma, S., Steensma, T. D., Kreukels, B. P. C., Cohen-Kettenis, P. T., de Vries, A. L. C., den Heijer, M., & Wiepjes, C. M. (2023). Children and adolescents in the Amsterdam Cohort of Gender Dysphoria: trends in diagnostic- and treatment trajectories during the first 20 years of the Dutch Protocol. *The journal of sexual medicine*, *20*(3), 398–409.

Wiepjes, C. M., Nota, N. M., de Blok, C. J. M., Klaver, M., de Vries, A. L. C., Wensing-Kruger, S. A., de Jongh, R. T., Bouman, M. B., Steensma, T. D., Cohen-Kettenis, P., Gooren, L. J. G., Kreukels, B. P. C., & den Heijer, M. (2018). The Amsterdam Cohort of Gender Dysphoria Study (1972-2015): Trends in Prevalence, Treatment, and Regrets. *The journal of sexual medicine*, *15*(4), 582–590.

Wittich, C. M., Burkle, C. M., & Lanier, W. L. (2012). Ten common questions (and their answers) about off-label drug use. *Mayo Clinic proceedings*, *87*(10), 982–990.

World Health Organization. (2018). Gender Incongruence. In International Classification of Diseases, 11th Revision. https://icd.who.int/browse11/l-m/en#/http%3a%2f%2fid.who.int%2ficd%2fentity%2f411470068.